

REMARKS

STATUS OF THE CLAIMS

By this Amendment, claims 1-7 are canceled, claims 8 -11 are amended and new claims 14-26 are added. Claims 8-26 are currently pending. Support for the amendments to the claims and the new claims can be found in the originally filed specification and claims. No new matter has been added. Specifically, support for the amendment substructure of formula III, which is also found in formula I, can be found in the original circular structure as drawn and the written description found, *inter alia*, at page 2, line 33, to page 7, line 12, and the originally filed claims.

Applicants thank the Examiner for indicating that "[t]he elected species wherein one of Q and Q' is not [a] bond and X is an alkylene of C₂₋₆ is neither anticipated or rendered obvious by the art of record." (Office Action at 6.)

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

A. The Examiner Rejects Claims 1-6 and 8 Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 1-6 and 8 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because the claims have more than one period and the Markush groups are confusing. Applicants have canceled claims 1-7 and rewritten them as claims 14-20. Applicants respectfully submit that the new claims render this aspect of the rejection moot.

The Examiner rejects claim 8 for failing to recite a quantitative limitation. Claim 8 has been amended as suggested by the Examiner.

The Examiner also rejects the claims because the substructure of formula III (ring structure substituted with D) is unclear because it is a 10-member ring structure, but is defined as possibly being any of several ring structures, including, for example, 5- to 10-membered, mono- or bicyclic, carbocyclic aryl, or heterocyclic. In an effort to clarify the ring structure, Applicants have amended formula I and formula III in the specification and claims to clarify that the ring structure B, together with D and the two carbon atoms to which D is attached, can be a 5- to a 10-membered ring. In particular, Applicants have revised the substructure of formula III, and its corresponding section in formula I, so that the ring structure can be of various carbon atoms as presently defined by the claimed invention. Moreover, by drawing the ring structure as a circle, Applicants believe that one of ordinary skill in the art reading the claimed possible choices for the substructure of formula III would be readily able to draw several structures, including, for example, bicyclic, or monocyclic rings structures, that fit within the definitions provided for formula III. For this reason, Applicants respectfully submit that the amended formulae I and III more particularly point out the claimed invention.

Applicants are not willing to amend the claims to the elected species, phenyl, optionally substituted with R¹, because if the Examiner finds this species allowable, then the Examiner is required to expand the scope of her search to other species, such as, for example, pyridyl.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.

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**B. The Examiner Rejects Claims 9 and 10 Under
35 U.S.C. § 112, Second Paragraph**

The Examiner rejects claims 9 and 10 under 35 U.S.C. § 112, second paragraph. The Examiner rejects claim 9 for either being a duplicate of claim 8 or for failing to recite a quantitative relationship. Applicants have amended claim 9 to recite a quantitative relationship, as suggested by the Examiner.

The Examiner rejects claim 10 because some of the recited conditions are pathology-related and some are responses which may or may not be treatable. Additionally, the Examiner indicated that the terms “associated with” and “for example” were not appropriate claim terminology. Claim 10 has been amended and new claim 24 has been added to recite treatable medical conditions. New claims 21-22 and 25-26 have been added to more particularly point out and distinctly claim the medical conditions originally recited in claim 10.

In view of the foregoing amendments, reconsideration and withdrawal of these section 112, second paragraph, rejections are respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

**A. The Examiner Rejects Claim 10 Under
35 U.S.C. § 112, First Paragraph**

The Examiner rejects claim 10 under 35 U.S.C. § 112, first paragraph, as failing to enable a method of treating multi-organ failure, certain viral infections, cancer, myocardial infarction, respiratory distress syndrome, etc. Claim 10 has been amended so that it no longer recites these medical conditions. Claims 21 and 22 have been added to clarify that these medical conditions may result in thrombosis or restenosis.

In view of these amendments, reconsideration and withdrawal of the rejection are respectfully requested.

**B. The Examiner Rejects Claim 11 Under
35 U.S.C. § 112, First Paragraph**

The Examiner rejects claim 11 under 35 U.S.C. § 112, first paragraph, as failing to enable all prodrugs, while providing enablement for making and using specific prodrugs, such as in claims 12 and 13. Without acquiescing in the rejection, and solely in an effort to advance prosecution, Applicants have amended claim 11 so that it recites that the prodrug is chosen from an acyl prodrug, a carbamate prodrug, an ester prodrug, and an amide prodrug.

REJECTION UNDER 35 U.S.C. § 102(f)

The Examiner rejects claims 1-6 under 35 U.S.C. § 102(f) over the following abstracts identified as CA:136:210039, CA:120:269926, CA91:193292, CA137:201331, and CA132:279106. Claims 1-6 have been canceled, but Applicants will address this rejection as it pertains to new claims 14-19. Applicants deny that the claimed invention was derived from another.

CA136:210039 is an abstract of a journal article published in 2001 - Levesque, Sophie, *et al.*, "Novel Bicyclic Lactam Inhibitors Of Thrombin: Potency And Selectivity Optimization Through P1 Residues," *Bioorganic & Medicinal Chemistry Letters*, 11(24):3161-3164 (2001). CA120:269926 is an abstract of European Patent Application No. 560613, published September 15, 1993. CA91:193292 is an abstract of a Japanese Patent Application published in 1979, and assigned to Taiho Yakuin Kogyo K.K. CA132:279106 is an abstract of WO 00/20358 published on April 13, 2000,

assigned to Agouron Pharmaceuticals, Inc. CA137:201331 is an abstract of WO 02/66446, published on August 29, 2002, assigned to Aventis Pharmaceuticals.

The Examiner argues that each of these disclose a compound that anticipates the claims and therefore the "issue of who is the first to invent such inventive concept as found" in the references "for which the specification did not disclose but are [sic] evidenced that 'another' was in possession of the claims." (Office Action at 5.)

Proving derivation under § 102(f) requires showing that: (a) the subject matter at issue was conceived in its entirety by another, and (b) this conception was communicated to the applicant for patent before the applicant's earliest date of invention. *Kilbey v. Thiele*, 199 U.S.P.Q. 290, 294 (Bd. Pat. Int. 1978); *see also New England Braiding Co. v. A.W. Chesterton Co.*, 970 F.2d 878, 883, 23 U.S.P.Q.2d 1622, 1626 (Fed. Cir. 1992); *Gambro Lundia AB v. Baxter Healthcare Corp.*, 110 F.3d 1573, 1578, 42 U.S.P.Q.2d 1378 (Fed. Cir. 1997) (applying the principles discussed above in reversing the district court's judgment that the patent in suit was invalid for derivation); *Ex parte Andersen*, 212 U.S.P.Q. 100, 102 (Bd. Pat. App. 1981). Applicants respectfully submit that the Examiner has failed to make either of the required showings.

With regard to all of the cited abstracts, the Examiner has failed to establish 1) that the claimed compound was conceived in its entirety by someone other than the Applicants, and 2) that the claimed compound was communicated to Applicants before their earliest date of invention, which is at least December 6, 2000, the filing date of the European Patent Application to which Applicants claim priority. In particular, Applicants note that CA136:210039 and CA137:201331 were both published after Applicants'

earliest date of invention, and therefore it seems improbable that their disclosed subject matter could have been communicated to Applicants prior to Applicants' earliest date of invention.

Moreover, M.P.E.P. § 2137 states:

Where there is a published article identifying authorship or a patent identifying the inventorship that discloses subject matter being claimed in an application undergoing examination, the designation of authorship or inventorship does not raise a presumption of inventorship with respect to the subject matter disclosed in the article or with respect to the subject matter disclosed but not claimed in the patent so as to justify a rejection under 35 U.S.C. § 102(f).

(8th ed. 2001) (emphasis added and internal citations omitted). Applicants respectfully submit that the cited abstracts have not raised a presumption of inventorship that justifies a rejection under 35 U.S.C. § 102(f).

Moreover, all of CA120:269926, CA91:193292, and CA132:279106 fail to teach a compound of formula I wherein R₀ is a phenyl or a mono- or bicyclic 5- to 10-membered heteroaryl, as presently claimed. Moreover, they do not teach or suggest a compound of the formula (I) wherein Q and Q' are different and are a direct bond or -O-, as presently claimed. Also, they do not teach or suggest a compound of the formula (I) wherein X is a (C₁-C₆)-alkylene, as presently claimed.

For at least the foregoing reasons, the Examiner has failed to establish that Applicants did not themselves invent the subject matter sought to be patented. Reconsideration and withdrawal of the rejection are respectfully requested.

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REJECTION UNDER 35 U.S.C. § 103

1. Beight in view of Klein

The Examiner rejects claims 1-13 under 35 U.S.C. § 103(a) over U.S. Patent No. 6,417,200 to Beight *et al.* ("Beight") in view of U.S. Patent Publication Application No. 2002/0016339 to Klein *et al.* ("Klein"). Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, the prior art references when combined must teach or suggest all the claim elements. M.P.E.P. § 2143 (8th ed. 2001). Applicants respectfully submit that the Examiner has failed to establish this requirement.

A. The Combination of Beight and Klein Does Not Teach or Suggest All the Claim Elements

The Examiner argues that Beight teaches "all the elements of the claims **except** the compounds are position isomer [sic] without an alkylene linker (see col. 47-48, examples 35-36)." (Office Action at 5, emphasis in original.¹) The Examiner relies on Klein for teaching that "3- or 4-substitution on the piperidinyl ring and insertion of a substituted alkylene chain between rings are optional choices" and refers to pages 12-13. (*Id.* at 5-6.) The Examiner argues that one of ordinary skill in the art would find the instant claims obvious "because the skilled person is deemed to be aware of all the pertinent art in the field." (*Id.*) In particular, the Examiner argues that the references

¹ In the original Office Action, the Examiner at the bottom of page 5, rejects the claims over "Beight *et al.* US 6,427,200" but then discusses "Ackerman *et al.* '436." Applicants telephoned the Examiner and requested clarification as to which reference the Examiner was rejecting the claims over. Moreover, Applicants indicated that if the Examiner was rejecting the claims over "Ackerman *et al.* '436", then it was unclear what this reference was because a full patent number had not been provided, and had never been cited on a Form PTO-1449 or PTO-892. The Examiner faxed to Applicants on June 9, 2003, a "correct version of office action in file." This corrected office action rejected the claims over Beight and discussed Beight at the bottom of page 5. Applicants have traversed the rejection based upon the corrected version of the Office Action.

place the “optional choices of substitution at three or four position compounds and the modification by inserting alkylene chains in the possession of artisan in the field.” (*Id.*)

Beight does not teach or suggest all the claim elements. In particular, Beight does not teach or suggest a compound of formula (I), wherein R_0 is chosen from a phenyl and a mono- or bicyclic 5- to 10-membered heteroaryl, as presently claimed. Moreover, Beight does not teach or suggest a compound of the formula (I) wherein Q and Q' are different and are chosen from a direct bond and -O-, as presently claimed. Also, Beight does not teach or suggest a compound of the formula (I) wherein X is a (C_1-C_6) -alkylene, as presently claimed.

Beight teaches a phenyl ring that is para-substituted. Beight does not teach or suggest a compound of the formula (I) wherein the substructure of formula III is a ring structure wherein D is inserted into the ring structure between two substituent groups on the ring, such as in a meta-substituted ring structure.

Additionally, Beight does not teach or suggest the elected species for V, *i.e.*, a compound of formula (I) wherein the nitrogen is singly bonded to a carbon atom, wherein the carbon atom is singly bonded to a substituent A and a substituent L. In particular, Beight does not teach or suggest a substituent L chosen from a direct bond and a (C_1-C_3) -alkylene, as presently claimed.

Klein does not overcome the deficiencies of Beight. Klein does not teach or suggest a compound of formula (I), wherein R_0 is chosen from a phenyl, wherein the phenyl is mono-, di- or trisubstituted independently of one another by R^2 , and a mono- or bicyclic 5- to 10-membered heteroaryl, as presently claimed. Moreover, Klein does not teach or suggest a compound of the formula (I) wherein Q and Q' are different and

are chosen from a direct bond and -O-, as presently claimed. Also, Klein does not teach or suggest a compound of the formula (I) wherein X is a (C₁-C₆)-alkylene, as presently claimed.

Klein teaches a phenyl ring that is para-substituted. Klein does not teach or suggest a compound of the formula (I) wherein the substructure of formula III is a ring structure wherein D is inserted into the ring structure between two substituent groups on the ring, such as in a meta-substituted ring structure.

For at least these reasons, none of the references, alone or in combination, would have rendered obvious the claimed invention.

B. The Examiner Improperly Refers to Another Patent Not of Record

The Examiner also argues that "[t]he modification of one known compound i.e., Ackerman '436 with attributes of another known compound i.e., Klein '339 is prima facie obvious." (*Id.* at 6, in the corrected Office Action.) Applicants do not know what reference the Examiner is referring to by "Ackerman '436" and presume she means Beight. If this presumption is not correct, Applicants request that the Examiner issue a new nonfinal Office Action, thereby providing Applicants with an opportunity to respond fully to this reference.

2. Klein in view of Beight

The Examiner rejects claims 1-13 under 35 U.S.C. § 103(a) over U.S. Patent Publication Application No. 2002/0016339 to Klein in view of U.S. Patent No. 6,417,200 to Beight. Applicants respectfully traverse the rejection.

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To establish a *prima facie* case of obviousness, the prior art references when combined must teach or suggest all the claim elements. M.P.E.P. § 2143 (8th ed. 2001). Applicants respectfully submit that the Examiner has failed to establish this requirement.

Both of these references were discussed in detail above. Applicants respectfully submit that, for the reasons discussed above, the combination of references fails to teach or suggest all the claim elements. Specifically, neither reference teaches or suggests that claimed compound of formula (I) wherein R₀, Q, Q', X, and D are as presently defined.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration of this application and the timely allowance of the pending claims.

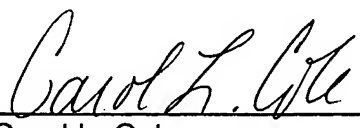
Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: August 12, 2003

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